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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/915,780	07/26/2001	Harn-Jing Terng	12674-003001	6948
26161	7590	12/03/2004	EXAMINER	
FISH & RICHARDSON PC 225 FRANKLIN ST BOSTON, MA 02110			TUNG, JOYCE	
			ART UNIT	PAPER NUMBER

1637

DATE MAILED: 12/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.

09/915,780

Applicant(s)

TERNG ET AL.

Examiner

Joyce Tung

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 10 November 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☐ The a) ☐ affidavit, b) ☐ exhibit, or c) ☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: 1-9 and 23-36.

Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.
10. ☐ Other: _____

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The applicant's response filed 11/10/2004 to the Office action has been entered. Claims 1-36 are pending. Claims 10-22 were withdrawn and claims 1-9 and 23-26 are now under examination.

1. Claims 1-9 and 23-36 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention since the newly added limitation "an unlabeled" discrimination primer has no support in the specification. Thus, it constitutes new matter.

Regarding the rejection of claims 1-9 and 23-36 for containing new mater, there were three new matter issues during the prosecution of this application so far. The first one was due to the language "wherein the first binding member is not labeled directly or indirectly ..." in the response filed March 10, 2003. The second one was due to the phrase "the first binding member is not labeled" added in the response filed July 18, 2003. The third one was due to the new limitation 'unlabeled' discrimination primer in claims 1 and 23 added in the last response filed June 7, 2004.

The response filed 11/10/2004 indicates that on page 8, lines 4-5 of the specification, there is the support for the new limitation 'unlabeled' discrimination primer. However, the support is not for the new limitation 'unlabeled' discrimination primer. Thus, the rejection is maintained.

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The new matter issue raised in the Advisory action dated September 3, 2003 was due to the phrase "the first binding member is not labeled" which is different from the phrase 'unlabeled' discrimination primer. Clarification is required.

2. Claims 1-4, 6-8, 23-26, 30 and 32-36 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Drazen et al. (6,156,503) in view of Ugozzoli et al. (DATA, 1992, Vol. 9(4), pg. 107-112).

Drazen et al. disclose a method and kit of identifying individuals at risk for an adverse response to β -agonist therapy (See column 1, lines 51-54). The method involves using allelic specific primer which has the same structure as the structure of the claimed discrimination primer (See column 11, lines 12-26) except the primer of Drazen et al. does not comprise a binding member covalently bonded to the 5' end of the primer. The primer of Drazen et al. has a mismatch at penultimate position from the 3' end (See column 11, lines 17-26) and a segment of nucleotide located immediately 5' to the second base is complementary to a part of target nucleic acid (the nucleic acid) (See column 11, lines 17-26).

Drazen et al. also disclose a kit to include primer set capable of amplifying and distinguish the allele specific gene (See column 4, lines 25-35).

Drazen et al. do not disclose that the primer comprises a binding member of a specific binding pair covalently bonded to the 5' end of the primer and the binding member is an oligonucleotide which is not complementary to any part of the nucleic acid.

Ugozzoli et al. disclose a method for determining whether a particular nucleic acid sequence is present in a sample. The method applies an allele-specific primer, which has 5' portion complementary to a different preselected nucleic acid sequence (See pg. 107, column 1,

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the abstract). The 5' portion is an oligonucleotide 6 to 50 nucleotides in length (See pg. 110, fig. 1). And there is an capturing nucleic acid sequence immobilized on the solid support (See pg. 110, fig. 1)

The limitations of claim 1 are interpreted as there is a first binding member of a specific binding pair located at 5' terminus which is the same as the 5' portion of the primer of Ugozzoli et al. (See pg. 107, column 1, the abstract) and a second binding member affixed on a solid substrate which is the same capturing nucleic acid sequence immobilized on the solid support of Ugozzoli et al. (See pg. 110, fig. 1). Therefore, the teachings of Drazen et al. in view of Ugozzoli et al. suggest the limitations of instant claims.

One of ordinary skill in the art would have been motivated to modify the primer of Drazen et al. by applying the 5' portion of the primer of Ugozzoli et al. for making an discrimination primer for amplifying a first base at a position suspected of a polymorphism and a second base immediately 3' to the first base. The motivation is that by using the binding member of a specific binding pair at 5' end of the primer, it allows the primer-extension product to be immobilized on a solid support by hybridization and it makes the method more specific and offers a valid alternative to study DNA polymorphism (See pg. 111, column 2, third paragraph). It would have been prima facie obvious to make the primer having a first binding member included in a specific binding pair located at the 5' portion which is not complementary to any part of the nucleic acid.

The response argues that claim 1 is specifically limited to a discrimination primer for PCR amplification only and does not cover that for primer extension. However, regardless of the

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discrimination primer or extension primer, the limitations of the primer claimed in the instant claims read on the teachings of Drazen et al. in view of the teachings of Ugozzoli et al.

Therefore the rejection is maintained.

3. Regarding the Declaration by Dr. Shin-Hwan Wang under 37 CFR 1.132 filed June 7, 2004 which is insufficient to overcome the rejection of claims 1-4, 6-8, 23-26, 30 and 32-36 based upon the teachings of Drazen et al. in view of the teachings of Ugozzoli et al as set forth in the office action mailed 12/3/2003 because:

The response argues that the primer having the above-mentioned ugozzoli 5'X portion did not work as a PCR amplification to generate specific amplification products, while the primer disclosed in the instant application (SEQ ID NO: 2) worked. However, SEQ ID NO: 2 was not cited in the claims. Thus, the Declaration is insufficient to overcome the rejection of the claims.

4. Claims 5, 9, 27-29 and 31 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Drazen et al. (6,156,503) in view of Ugozzoli et al. (DATA, 1992, Vol. 9(4), pg. 107-112) as applied to claims 1-4, 6-8, 23-26, 30 and 32-36 above, and further in view of Drmanac et al. (6,383,742, issued May 7, 2002).

The teachings of Drazen et al. and Ugozzoli et al. are set forth in section 2 above. Drazen et al. and Ugozzoli et al. do not disclose the binding member, which is peptide and the primer, is labeled.

Drmanac et al. disclose a method of detecting a target nucleic acid species involving using labeled probe (See the Abstract). The label can be ligands which can serve as specific

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binding members to a labeled antibody, chemiluminescers, enzymes, antibodies which can serve as a specific binding pair member for a labeled ligand (See column 18, lines 64-67 to column 19, lines 1-4). The antibodies and enzymes are peptide.

Therefore one of ordinary skill in the art would have been motivated to modify the primer of Drazen et al. by applying the antibody as a binding member as taught by Drmanac et al. (See column 18, lines 64-67 to column 19, lines 1-4 and column 22, lines 1-14) at 5' terminus of the primer. The motivation is that by using the binding member of a specific binding pair at 5' end of the nucleic acid primer, a small number of nucleic acid samples can be fast identified (See column 6, lines 64-67). It would have been prima facie obvious to make the discrimination primer with a peptide-binding member at 5' terminus.

The response argues that the discrimination primer recited in claim 1 and the first primer recited in claims 1 and 23 are unlabeled. However, there is a second primer cited in claim 28, which is labeled at 5' end. This is the reason applying the teachings of Drmanac et al. Thus, the combination of the references renders claims obvious and the rejection is maintained.

Summary

5. No claims are allowable.

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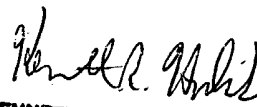
6. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

7. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung
November 29, 2004


KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

12/1/04